REMARKS

Claims 1-6 are pending in this application. Claims 1-6 have been rejected. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Claim rejections under 35 USC 103

Claims 1-6 have been rejected under 35 U.S.C. §103 (a) as being unpatentable over Anderson et al (U.S. Patent No. 5,994,104) in view of Ruoslahti et al. (U.S. Patent No. 6,180,084). The Examiner suggests that Anderson et al. teach the use of IL-12 fusion proteins (*e.g.*, a fusion with B7) for cancer therapy and provides the motivation or suggestion for targeting rIL12 to the site of a tumor. The Examiner further suggests that Ruoslahti et al. teach use of RGD sequence to target α_v-integrins selectively expressed in the tumor blood vessels of patients and the administration of a chemotherapeutic agent linked to a tumor homing molecule for treating a tumor. It is further suggested that it would have been obvious to one of ordinary skill in the art to operably link IL-12 disclosed in Anderson et al. to a RGD-containing peptide described in Ruoslahti et al. to produce a fusion protein conjugate capable of binding to α_v-integrin receptors on the surface of tumor blood vessels to destroy the blood vessels with greater efficacy and cause tumor necrosis with reasonable success, because Anderson et al. provides the motivation in that rIL-12 has been demonstrated to have potent anti-tumor effects and to have the best therapeutic effects when delivered at

the site of tumor, in treating a tumor. Applicants respectfully traverse this rejection.

Applicants respectfully disagree with the Examiner's analysis of Anderson et al. This reference does **not** teach a fusion between B7 and IL-12. Rather, Anderson et al. teach a Flexi-12 fusion protein comprising the p35 and p40 subunits of IL-12 wherein the subunits are covalently joined by a linker peptide (see page column 5, first full paragraph). Anderson et al. further teach that using a single promoter, the Flexi-12 and B7 coding sequences can be co-transcribed on the same mRNA molecule. However, this reference specifically indicates that by utilizing an internal ribosome entry site (IRES), the B7 and Flex-12 proteins are translated as **two independent** proteins, not as a fusion protein (see column 8, lines 51-63). Co-transcription and independent translation of Flex-12 and B7 in recombinant cells is further exemplified in columns 22-24, wherein the IL-12 is found to be expressed intracellularly and B7 on the cell surface (see, in particular column 23, lines 40-46). Further, this reference does not teach or suggest creating direct fusion proteins comprising B7 and either the p35 or p40 subunit or the Flexi-12 protein.

While the reference of Ruoslahti et al. teaches a tumor homing peptide such as RGD conjugated to a therapeutic agent for treating a tumor, nowhere does this reference teach or suggest that the therapeutic agent is IL-12. Therefore, this reference does not remedy the deficiencies of the primary reference of Anderson et al.

Accordingly, these references provide no motivation or suggestion to combine their teachings to arrive at a fusion protein comprising a mammalian interleukin-12 operably linked to an RGD-

containing peptide. Nor do these references lend any reasonable expectation of success because they do not teach fusing an IL-12 subunit with any other non-IL-12 protein. It is only in view of teachings of the instant application that one of skill would be motivated to combine the teachings of the cited references to arrive at the instant inventive fusion proteins. MPEP § 2143 states that the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicants' disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Because the combined references do not meet the requirements set forth by MPEP § 2143 it is respectfully requested that this rejection be withdrawn.

II. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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